

PATENT COOPERATION TREATY

Received
17 MRS. 2006
PCT LifeCyclePharma A/S

From the INTERNATIONAL SEARCHING AUTHORITY

To:
LIFECYCLE PHARMA A/S
Attn. Jorsboe, Anne-Marie
Kogle Allé 4
DK-2970 Horsholm
DENMARK

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year)	17/03/2006
Applicant's or agent's file reference 00301-WO10	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/DK2004/000836	International filing date (day/month/year) 01/12/2004
Applicant LIFECYCLE PHARMA A/S	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Marthe Oldendorf

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44).

Applicant's or agent's file reference 00301-WO10	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/DK2004/000836	International filing date (day/month/year) 01/12/2004	(Earliest) Priority Date (day/month/year) 01/12/2003
Applicant LIFECYCLE PHARMA A/S		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☐ Unity of invention is lacking (see Box III).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK2004/000836

A. CLASSIFICATION OF SUBJECT MATTER

A61K9/16 A61K9/20 A61K31/4418

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/180355 A1 (LEONARDI AMEDEO ET AL) 25 September 2003 (2003-09-25) cited in the application page 5, paragraph 56 - paragraph 59 page 6; table 3	1,4,5,9, 13-20, 22-24, 31-41, 47,48
X	WO 03/014084 A (RECORDATI IRELAND LIMITED) 20 February 2003 (2003-02-20) claims 1-5	1,4

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

3 March 2006

Date of mailing of the international search report

17/03/2006

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3018

Authorized officer

Muller, S

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/DK2004/000836

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003180355 A1	25-09-2003	NONE	
WO 03014084 A	20-02-2003	AT 307114 T	15-11-2005
		BR 0211739 A	28-09-2004
		CN 1538957 A	20-10-2004
		EA 5673 B1	28-04-2005
		EP 1432683 A1	30-06-2004
		ES 2212759 T1	01-08-2004
		HR 20040156 A2	31-08-2004
		HU 0401163 A2	28-09-2004
		IT MI20011726 A1	06-02-2003
		JP 2005504045 T	10-02-2005
		MA 27133 A1	03-01-2005
		MX PA04001069 A	17-02-2005
		NZ 531558 A	23-12-2005
		ZA 200401806 A	18-04-2005

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/DK2004/000836

International filing date (day/month/year)
01.12.2004

Priority date (day/month/year)
01.12.2003

International Patent Classification (IPC) or both national classification and IPC
INV. A61K9/16 A61K9/20 A61K31/4418

Applicant
LIFECYCLE PHARMA AS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Muller, S

Telephone No. +31 70 340-2080



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/DK2004/000836**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/DK2004/000836

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2,3,6-8,10-12,21,25-30,34,42-46
	No: Claims	1,4,5,9,13-20,22-24,31-33,35-41,47,48
Inventive step (IS)	Yes: Claims	2,3,6-8,10-12,21,25-30,42-46
	No: Claims	1,4,5,9,13-20,22-24,31-33,34-41,47,48
Industrial applicability (IA)	Yes: Claims	1-48
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/DK2004/000836

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Cited Documents

Reference is made to the following documents:

- D1: US 2003/180355 A1 (LEONARDI AMEDEO ET AL) 25 September 2003 (2003-09-25)
D2: WO 03/014084 A (RECORDATI IRELAND LIMITED) 20 February 2003 (2003-02-20)

2. Clarity (Art. 6 PCT)

The expressions (release) "in a controlled manner" in independent claim 1 and "ambient temperature" in claims 2-4 are vague and indefinite and leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of said claims unclear, Article 6 PCT.

3. Novelty (Art. 33(2) PCT)

D1 discloses (see page 5, paragraphs 56-59 and page 6, table 3) a 10mg lercanidipine coated tablet formulation comprising: a) a core comprising lercanidipine HCl, lactose, mcc, sodium starch glycolate, povidone, Mg stearate and b) a coating comprising hypromellose, talc, titanium dioxide, Macrogol 6000 and ferric oxide. The subject-matter of claims 1,5,9,13-20,22-24,31-33,35-41,47,48 is therefore not new in view of D1 (Article 33(2) PCT).

D2 discloses (see claims 1-5) an aqueous suspension of lercanidipine. The subject-matter of claims 1 and 4 is therefore not new in view of D2 (Article 33(2) PCT).

4. Inventive Step (Art. 33(3) PCT)

Claims 1,16-20,22-24,31-33,35-41,47,48 not being new are also not inventive (Article 33(3) PCT).

Regarding dependent claims 2,3,6-8,10-12,21,25-30,34,42-44, the Applicant should note that a claim can only be recognized as inventive if the technical features which render that claim novel solve a particular technical problem in a non-obvious manner.

Regarding independent claims 45 and 46, the following Problem-Solution-Approach reasoning could be made:

D1 is considered as closest prior art.

It discloses (see page 5, paragraphs 56-59 and page 6, table 3) a 10mg lecanidipine coated tablet formulation comprising: a) a core comprising lecanidipine HCl, lactose, mcc, sodium starch glycolate, povidone, Mg stearate and b) a coating comprising hypromellose, talc, titanium dioxide, Macrogol 6000 and ferric oxide prepared by conventional methods.

The subject-matter of claims 45 and 46 differs from D1 in a completely new process for preparing pharmaceutical compositions comprising a step where lecanidipine is dissolved, suspended or dispersed in a liquid vehicle.

Pharmaceutical compositions produced by this new process achieve (see page 1, lines 3-8) slow release of lecanidipine over an extended period of time, sufficient bioavailability to enable a once daily dosing, reduced food effect, and are expected to reduce peak related side effects.

The objective problem of the application may therefore be regarded as the provision of a new process for producing improved pharmaceutical compositions comprising lecanidipine.

No other document in the prior art discloses pharmaceutical compositions comprising lecanidipine.

The subject-matter of claims 45 and 46 therefore appears to be inventive over the prior art (Article 33(3) PCT).

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/DK2004/000836

5. Industrial Applicability (Art. 33(4) PCT)

Claims 1-48 satisfy the criterion of industrial applicability set forth in Article 33(4) PCT.